News and Views from the Literature

Urinary Tract Infection

Immunological Based Therapies for Urinary Tract Infection: The Future Is Almost Here!

Reviewed by J. Curtis Nickel, MD, FRCSC
Department of Urology, Queen's University, Kingston, Ontario, Canada

[*Rev Urol.* 2002;4(4):196–197]

Urinary tract infections (UTIs) in women with normal urinary tract anatomy remain a clinical problem, despite the plethora of antibiotics released over the last two decades. Forty to fifty percent of women will suffer a UTI in their lifetime; 25%–50% will recur within several months; and 2%–10% suffer multiple recurrent episodes.[1] Repeat treatment with antibiotics is necessary, and many women develop significant side effects. Antibiotic-resistant organisms are increasing in prevalence, making many of the traditional front-line antimicrobial-based therapies, such as penicillins, sulfas, and even trimethoprim-sulfamethoxazole ineffective. As far as antibiotic therapy for UTI is concerned, there has been no major improvement in treatment for the last decade, and rising resistance rates to even our second- and third-line antibiotics is becoming a clinical problem. We have no expectations of major breakthroughs in antimicrobial therapy for UTIs in the near future.

However, the use of vaccines to prevent UTIs in susceptible women is an exciting development. Although once appearing distant on the clinical horizon, it is now coming close to being reality. The hypothesis on which UTI vaccine development is based is that increased urinary antibody can prevent bacterial adherence to urinary epithelium, inhibit the biological activity of bacterial virulence factors, and therefore decrease infectivity or persistence. Two recent reports outlining the success of oral and vaginal preparations that stimulate the patients' own immune system may provide the clinical breakthrough we are looking for.

Although once appearing distant on the clinical horizon, the use of vaccines for the prevention of urinary tract infection is now coming close to being reality.

Vaginal Mucosal Immunization for Recurrent Urinary Tract Infection: Extended Phase II Clinical Trial

Uehling DT, Hopkins WJ, Beierle LM, et al.
J Infect Dis. 2002;183(suppl 1):S81–S83.

This research group previously demonstrated with animal models that mucosal immunity could be stimulated through vaginal immunization, and they have furthered their studies through a number of clinical trials. Women

receiving a whole-cell vaccine (SolcoUrovas, Solco, Basel, Switzerland) containing heat-killed bacteria from 10 human uropathogenic strains, including six *Escherichia coli* strains and one strain each of *Proteus mirabilis*, *Proteus morganii, Enterococcus faecalis*, and *Klebsiella pneumoniae*, had a significant delay in acquiring their first reinfection compared with women who were given placebo. In the trial reported here, the goal was to extend the protection period beyond 8 weeks (first randomized, placebo-controlled trial) by use of booster suppositories. The investigators randomized 36 patients to intermittent vaginal suppository treatments of vaccine or placebo; one group received real vaccine for 14 weeks (vaccine-vaccine), one group received real vaccine for 2 weeks and then placebo (vaccine-placebo), and the third group received placebo for 14 weeks (placebo-placebo). There were no reinfections in 50% of the vaccine-vaccine group, 25% of the vaccine-placebo group, and 17% of the placebo-placebo group. In patients with reinfections, the median times to reinfection were 46, 21, and 16 days, respectively, in these three groups. There were no significant side effects of treatment. Vaginal immunization for recurrent UTIs may someday be a safe and effective treatment method.

Prevention of Recurrent Urinary Infections with Immuno-Active *E. coli* fractions: A Meta-Analysis of Five Placebo-Controlled, Double-Blind Studies

Bauer HW, Rahlfs VW, Lauener PA, Blessmann GS.
Int J Antimicrob Agents. 2002;19:451–456.

The authors performed a meta-analysis of five studies over the last decade to evaluate the effect of an oral vaccine (Uro-Vaxom, Sanofi Winthrop GmbH, Munich, Germany) developed from a bacterial extract consisting of 18 uropathogenic *Escherichia coli* strains. The efficacy of this oral vaccine has actually been investigated in 12 studies, but only five were placebo-controlled, randomized, double-blind studies. The primary criterion in all studies was the number of recurrences per patient. The studies evaluated were all basically the same: 3 months' treatment with observation and a further observation period of 3 months without treatment. A total of 717 patients were enrolled and randomized in the five studies; 501 were subsequently evaluable. There was a statistically significant decrease in recurrences in patients treated with the oral vaccine compared with placebo in every study. The pooled odds ratio (2.28) demonstrated at least statistical proof for a relevant drug effect, of modest size at least. The number of UTIs in patients treated with this vaccine was 0.15–0.82 per year, which compares favorably with low-dose antimicrobial prophylaxis. The safety and tolerability of the oral vaccine was good, with no real difference in minor side effects compared to placebo and no serious side effects reported. Oral immunotherapy with this or similar products may turn out to be effective therapy in the prevention of UTIs.

Conclusion

Recurrent UTIs in women are currently being treated with episodic, physician-directed therapy, low-dose prophylaxis, postcoital therapy, and patient self-directed therapy. All these approaches employ antibiotics and are subject to resistance problems, side effects, and cost considerations. Immunotherapy, with a vaginal or oral preparation, may turn out to be an effective alternative to antibiotics in the prevention of recurrent UTIs. ■

References

1. Nickel JC. Urinary Tract Infections in Adults. In: Teichman JMH, ed. *20 Common Problems in Urology*. New York, NY: McGraw-Hill; 2001:63–76.

Erectile Dysfunction

Prescribing PDE5 Inhibitors: Who Is the "Normal" Man?

Reviewed by Jacob Rajfer, MD
UCLA School of Medicine and Division of Urology, Harbor-UCLA Medical Center, Los Angeles, CA

[*Rev Urol.* 2002;4(4):197–198]

Sex, sex, sex! Men are imprinted to think about it all the time—not only when they are awake, but also when asleep. As men age and their erectile function changes for the worse—in some men as early as their 20s and noticeably in 40% of men by the time they reach age 40—nocturnal erections follow suit. Ever since the phosphodiesterase type 5 (PDE5) inhibitors were released for clinical use for the treatment of erectile dysfunction (ED) in 1998, the mantra has always been that these drugs should only be used in men with ED and not in "normal" men. The fear has always been that these drugs will be "abused" by normal men. How was "abuse" defined? It was defined as making erections last longer and decreasing the refractory time between ejaculations.

As clinical experience with the use of PDE5 inhibitors has been gained over the past 4 years, the following have become apparent in men with ED: 1) that PDE5 inhibitors are not only effective in improving erectile function, but